

TOBACCO INDUSTRY RESEARCH COMMITTEE
350 FIFTH AVENUE NEW YORK 1, N. Y.

4 Budget Plan

Salaries (and overhead)
Expendable Supplies
Application For Research Grant

Overhead
Other

(travel and so on) Date: September 7, 1954

1. Name of Investigator: Principal Investigator Maurice H. Shulman, M.D.

2. Titles and Staff: Associate Investigators

Brenton R. Lutz, PhD. Professor of Biology
Chairman of the Department

George P. Fulton, Ph.D. Professor of Biology

3. Institution

& Address:

Department of Biology, Graduate School
Boston University - 755 Commonwealth Avenue
Boston 15, Massachusetts

4. Project or Subject:

Direct observations on blood vessels during exposure to the
9. Additional Requirement: constituents of cigarette and pipe smoke.

5. Detailed Plan of Procedure (Use reverse side if additional space is needed). We propose to use the membranous (mucous cheek pouch of the hamster for the direct observation of blood vessel activity in response to cigarette smoke and for motion picture recording by a technique which has been developed in this laboratory during the past fifteen years. This preparation has given significant results in investigations on thrombus formation, intravascular coagulation, in vivo effects of anticoagulants, vascular effects of corticosteroids, irradiation studies, the mechanism of petechial formation, and the effect of the ingredients of certain skin preparations. This method allows documentation at high magnification (1200 X) with kodachrome motion pictures taken through the microscope by means of transillumination. We have developed methods for taking cheek pouch blood pressures, blood sugars, electrolyte levels, electrocardiograms and blood volumes. We have done these procedures routinely in other projects and correlated them with direct observations.

The following are some of the aspects we plan to investigate:

1. Topical application of the constituents of smoke (paper and tobacco) in the dilutions naturally found.
2. Comparison of the results with the effects on the blood vessels when the same substances are respired.
3. Intravenous administration and also perfusion of these substances in known amounts by a method which by-passes such organs as the liver, lungs and kidneys. Since various substances entering the body parenterally are known to be destroyed or altered by various internal organs, a direct perfusion technique which by-passes the liver, lungs and kidneys may be instructive.
4. Effect of cigarette smoke on the nervous system and heart as shown by encephalography and electrocardiograms.
5. Possible vascular effects of tobacco smoke, such as changes in tendency for thrombus formation, vaso-motor thresholds, vascular fragility, electrolyte levels (potassium, sodium, calcium, magnesium, and permeability of cell membranes).

1003541166

Number 5 continued -

6. The preceding studies can be carried out from early life to old age, and the blood pressures followed. The life-span of the hamster is about two years.

7. Because of the short life span, the chronic effects can be determined. In fact, procedures can be carried out and recorded on the same animal from early maturity to old age.

Number 8 continued -

All technical personnel available. Research Associate to be selected from previous doctoral trainees. Special consultants in Biochemistry and Physics are available.

Facilities available:

Laboratories with services and basic equipment. Machine shop and electronic service.

Motion picture camera, projector and dark room facilities

Autotechnicon for tissue work.

Electrocardiographic equipment.

Animal rooms and cages

Equipment for isotope work and dosimetry (permeability studies.)

Electronic stimulator

1003541167

6. Budget Plan:

Salaries (and social security, 2%)	\$ 25,468.
Expendable Supplies	2,850.
Permanent Equipment	10,300.
Overhead	3,910.
Other	500.
(travel and communication)	\$ 43,028.00

7. Anticipated Duration of Work: 2 years (Second year, \$30,000)

8. Facilities and Staff Available:

Principal Investigator	\$ 5,000
2 Associate Investigators	5,000
Research Associate	5,000
Research Assistant	3,800
Photographic Technician	2,000 (part time)
Secretarial Assistant	1,200 (part time)
Animal care	1,000
Consultant fees	2,000
	\$ 25,000
(Please see extra paper)	

9. Additional Requirements:

None

10. Additional Information (Including relation of work to other projects and other sources of supply):

The proposed research on tobacco constituents is obviously related closely to our current projects (supported by the Public Health Service and the Atomic Energy Commission) such as the production and prevention of thromboembolism, the effects of ionizing radiations on blood vessels, the vascular effects of adrenalectomy and hypersteroidism, and the vascularization of tumors transplanted to the hamster cheek pouch. We have developed various techniques for taking chest cavity blood pressures, blood sugar, electrolyte levels, electrocardiograms and blood viscosity. We have done these procedures routinely in other projects and correlate them with direct observations.

The following are some of the aspects we plan to investigate:

1. Topical application of the constituents of smoke (paper and filter) in the hamster cheek pouch.
2. Comparison of the results with the effects on the blood vessels when the same constituents are respired.
3. Intravenous administration and also perfusion of these substances in hamster cheek pouches which bypass the lungs and kidneys. Since various substances entering the body are known to be destroyed or altered by various internal organs, a direct perfusion technique which bypasses the liver, lungs and kidneys may be instructive.
4. Effect of cigarette smoke on the nervous system and heart as shown by encephalography and electrocardiograms.
5. Possible vascular effects of tobacco smoke, such as changes in tendency for thrombosis or atherosclerosis.

Signature: Maurice H. Shulman, M.D.
Director, Division of Experimental Medicine
Business Office: Dr. Shulman

1003541168